

- (f) partitioning said pooled fragments to provide one or more selected subsets;
- (g) identifying a specific fragment from one or more selected subsets;
- (h) mapping the specific fragment to its original location; and
- (i) sequencing said specific fragment, thereby identifying a nucleic acid sequence.

59. The method of claim 58 wherein said one or more populations of nucleic acid molecules is genomic DNA.
60. The method of claim 59 wherein said genomic DNA is isolated from a plurality of cell types.
61. The method of claim 60 wherein said cell types are mixed tissue types.
62. The method of claim 58 wherein said one or more subpopulations of nucleic acid molecules are modified by at least one step selected from:
- i) digesting said nucleic acid molecules with at least two restriction endonucleases;
 - ii) ligating an adapter oligonucleotide to one or more ends of a digestion product; and
 - iii) amplifying a ligated product from a PCR-mediated amplification reaction.
63. The method of claim 58 further comprising amplifying one or more populations of nucleic acid molecules.
64. The method of claim 58 further comprising amplifying one or more subpopulations of nucleic acid molecules.
65. The method of claim 58 wherein said specific nucleic acid fragments are distinguishable from members of the library by physical and biochemical properties.
66. The method of claim 65 wherein said physical and biochemical properties are selected from molecular weight, molecular size, terminal nucleotide sequences, exact migratory pattern, ionic charge, or affinity.
67. The method of claim 58 wherein said specific nucleic acid fragments comprise a unique identifier.
68. The method of claim 58 wherein said specific fragments are identified by a sizing filter.

69. The method of claim 58 wherein said one or more populations of nucleic acids are isolated from pooled or unpooled samples.
70. The method according to claim 58 wherein said array is traced on a pooling map.
71. The method according to claim 58 further comprising correlating said selected subsets to said pooling map prior to sequencing.
72. A method of identifying a nucleic acid sequence, the method comprising:
- (a) providing one or more populations of nucleic acid molecules comprising at least one set of nucleic acid sequences;
 - (b) digesting the one or more populations of nucleic acid molecules with one or more restriction enzymes to produce one or more subpopulations of nucleic acid molecules;
 - (c) partitioning said subpopulations to produce one or more partitioned fractions;
 - (d) constructing a library from said partitioned fractions wherein said library comprises specific nucleic acid fragments distributed in an array;
 - (e) pooling said specific fragments from said library to provide pooled fragments that are mapped;
 - (f) sizing said pooled fragments to provide multiplex sized sets;
 - (g) deconvoluting said multiplexed sets; and
 - (h) identifying a nucleic acid sequence from said multiplexed sets.
73. A method of identifying a nucleic acid sequence, the method comprising:
- (a) digesting one or more populations of nucleic acid molecules with one or more restriction enzymes to produce one or more subpopulations of nucleic acid molecules;
 - (b) pooling said subpopulations of nucleic acid molecules;
 - (c) fractionating said pooled subpopulations to produce a plurality of fractions;
 - (d) cloning said fractions to provide a library of fractions wherein said library comprises specific nucleic acid fragments distributed in an array;
 - (e) sizing said pooled fragments to provide multiplex sized sets;
 - (g) deconvoluting said multiplexed sets; and
 - (h) sequencing one or more fragments in said multiplex set to provide a nucleic acid sequence.

74. The method of claim 58, wherein the population of nucleic acid molecules is amplified using a first primer and a second primer.
75. The method of claim 58, wherein said library is generated from partitioned fractions selected from the 5' end of nucleic acid molecules, the internal regions of nucleic acid molecules, or the 3' end of nucleic acid molecules.
76. The method of claim 58, wherein the population of nucleic acid molecules is provided as a plurality of cDNA molecules
77. The method of claim 58, wherein the population of nucleic acid molecules comprises a normalized population of nucleic acids.
78. The method of claim 58, wherein partitioned fractions are separated by size.
79. The method of claim 58 wherein said partitioning step is electrophoretic separation of said one or more subpopulations.
80. The method of claim 79 wherein the partitioning step is accomplished by polyacrylamide gel electrophoresis.
81. The method of claim 79 wherein the partitioning step is accomplished by agarose gel electrophoresis.
82. The method of claim 58 wherein the subpopulations of nucleic acid molecules differ by 20 or fewer nucleotides in length.
83. The method of claim 58 wherein the subpopulations of nucleic acid molecules differ by 15 or fewer nucleotides in length.
84. The method of claim 58 wherein the subpopulations of nucleic acid molecules differ by 12 or fewer nucleotides in length.
85. The method of claim 58 wherein the subpopulations of nucleic acid molecules differ by 8 or fewer nucleotides in length.
86. The method of claim 58 wherein the subpopulations of nucleic acid molecules differ by 6 or fewer nucleotides in length.
87. The method of claim 58, wherein the subpopulation of nucleic acid molecules comprises nucleic acids having terminal sequences identical to those produced by digestion of a nucleic acid molecule with one or more restriction endonucleases.

88. The method of claim 58, wherein the restriction endonuclease is a Type II or Type IIS restriction endonuclease.
89. The method of claim 88, wherein the restriction endonuclease recognizes a six nucleotide recognition sequence.
90. The method of claim 58, wherein the library is prepared by a process comprising:
- (a) ligating the one or more subpopulations of nucleic acid molecules to a vector to form a population of vector-insert nucleic acid molecules;
 - (b) transforming the population of vector-insert nucleic acid molecules into a host cell to form a library; and
 - (c) culturing the library under conditions that allow for at least some members of the library to be distinguished from other members of the library.

REMARKS

Upon entry of the amendment, claims 58-90 will be pending in the application. Claims 27-57 have been canceled by this response and new claims 58-90 have been added therefore. These new claims draw their support from the claims and figures as originally filed and generally throughout the specification. No new matter has been added.

The Examiner has withdrawn any objections or rejections based on 35 USC §112, second paragraph. The claims are rejected as obvious, on various grounds.

Rejections under 35 USC 103 (a) Overcome

Claims 27-42 and 47-55 are rejected by the Examiner as prima facie obvious over Kamb et al., U.S. Patent No. 6,020,240 ("Kamb") in view of Short et al., U.S. Patent No. 6,173,673 ("Short") and further in view of Okayama, Mol. Cell. Biol. 2:161-70 ("Okayama"). The rejection is traversed as applied to new claims 58-90 submitted herein.

In performing analysis for determining whether a claimed invention is prima facie obvious over the prior art (See MPEP Rev. 1, Feb. 2000, Section 2141):

- (A) The claimed invention must be considered as a whole;
- (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; [and]